

Substitute for Form 1449/A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 8

Complete if Known

Application Number	09/644,387
Filing Date	August 23, 2000
First Named Inventor	Gregory Agoston, et al.
Group Art Unit	1616
Examiner Name	Radio, B.
Attorney Docket Number	05213-0541 (43170-219662)

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
BB	AA	2,584,271	✓	Huffman, Max N.	02-05-1952	RECEIVED JAN 03 2003 TECH CENTER 180012900
	AB	2,846,453	✓	Hoehn, Willard M.	08-05-1958	
	AC	3,410,879	✓	Smith, Herchel, et. al.	11-12-1968	
	AD	3,470,218	✓	Farah, Basil S.	09-30-1969	
	AE	3,492,321	✓	Crabbe, Pierre	01-27-1970	
	AF	3,496,272		Kruger, Gunther (Identifier only)	02-17-1970	
	AG	3,956,348	✓	Hilscher, Jean-Claude	05-11-1976	
	AH	4,172,132	✓	Draper, Richard W., et al.	10-23-1979	
	AI	4,212,864	✓	Tax, Lambert J.W.M.	07-15-1980	
	AJ	4,307,086	✓	Tax, Lamber J.W.M.	12-22-1981	
	AK	4,522,758	✓	Ward, John S., et al.	06-11-1985	
	AL	4,743,597	✓	Javitt, Norman B., et al.	05-10-1988	
	AM	4,994,443	✓	Folkman, Moses, J., et al.	02-19-1991	
	AN	5,001,116	✓	Folkman, Moses J., et al.	03-19-1991	
	AO	5,504,074	✓	D'Amato, Robert J., et al.	04-02-1996	
	AP	5,135,919	✓	Folkman, J., et al.	08-04-1992	
	AQ	5,521,168		Clark, Abbot F.	05-28-1996	
	AR	5,504,074	✓	D'Amato, Robert J., et al.	04-02-1996	
	AS	5,521,168	✓	Clark, A.	05-28-1996	
	AT	5,621,124	✓	Seilz, Carsten, et al.	04-15-1997	
BB	AU	5,643,900	✓	Fotsis, Theodore, et al.	07-01-1997	
	AV	5,661,143	✓	D'Amato, Robert J., et al.	08-26-1997	
	AW	5,892,069	✓	D'Amato, Robert John, et al.	04-06-1999	
	AX	6,136,992	✓	Ram, S., et al.	10-24-2000	
	AY	6,200,966	✓	Stewart, Alastair G.	03-13-2001	

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁴
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
BB			WO 90/15816	✓	The UpJohn Company	12-27-1990		
	AZ		WO 93/03729	✓	Research Corporation Technologies, Inc.	03-04-1993		
	BA		WO 95/04535	✓	The Children's Medical Center Corporation	02-16-1995		
BB	BB		WO 98/40398	✓	Pharm-Eco Laboratories, Inc.	09-17-1998		
	BC		DE 3625315		Schering A.-G	01-28-1988	To assist English translation provided	
	BD		DE 1907330		Sandoz Ltd.	10-23-1969		

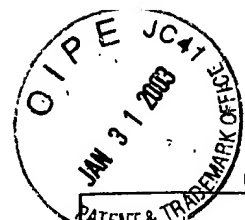
Examiner
Signature

Radio

Date
Considered

3/24/03

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.



Substitute for Form 1449/A/PTO		Complete if Known	
		Application Number	09/644,387
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Filing Date	August 23, 2000
		First Named Inventor	Gregory Agoston, et al.
		Group Art Unit	1616
		Examiner Name	Badio, B.
		Attorney Docket Number	05213-0541 (43170-219662)
Sheet	6	of	8

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
B.B.	GA	Nambara, T., et al., "Studies on Steroid Conjugates. III. New Syntheses of 2-Methoxyestrogens" <u>Chem. Pharm. Bull.</u> , Vol. 18, No. 3, pp. 474-480 (1970)	
	GB	Napolitano, et al., "11 Beta-Substituted Estradiol Derivatives. 2. Potential Carbon-11 and Iodine-Labeled Probes for the Estrogen Receptor", <u>J. Med. Chem.</u> , Vol. 38, No. 14, pp. 2774-2779 (July 7, 1995) (Abstract Only)	
	GC	Nishigaki, et al., "Anti-Proliferative Effect of 2-Methoxyestradiol on Cultured Smooth Muscle Cells from Rabbit Aorta", <u>Atherosclerosis</u> , Vol. 113, pp. 167-170 (1995)	
	GD	Numazawa M. et al., "Efficient Synthesis of 2-Methoxy- and 4-Methoxy-Estrogens" <u>J. Chem. Soc.</u> , pp. 533-534 (1983)	
	GE	Oppolzer, et al., "177. The Enantioselective Synthesis of (+)-Estradiol from 1,3-Dihydrobenzo[c]thiophene-2,2-dioxide by Successive Thermal SO ₂ -Extrusion and Cycloaddition Reactions", <u>Helvetica Chimica Acta</u> , Vol. 63, pp. 1703-1707 (1980)	
	GF	Parthasarathy, et al., "Antioxidant: A New Role for RU-486 and Related Compounds", <u>J. Clin. Invest.</u> , Vol. 94, No. 5, pp. 1990-1995 (1994) (Abstract Only)	
	GG	Paull, et al., "Identification of Novel Antimitotic Agents Acting at the Tubulin Level by Computer-assisted Evaluation of Differential Cytotoxicity Data", <u>Cancer Research</u> , Vol. 52, pp. 3892-3900 (July 15, 1992)	
	GH	Poli et al., "Tumor Necrosis Factor α Functions in an Autocrine Manner in the Induction of Human Immunodeficiency Virus Expression", <u>Proc. Natl. Acad. Sci. USA</u> , Vol. 87, pp. 782-785 (January 1990)	
	GI	Rao, et al., "Structural Specificity of Estrogens in the Induction of Mitotic Chromatid Non-Disjunction in Hela Cells", <u>Experimental Cell Research</u> , Vol. 48, pp. 71-81 (1967)	
	GJ	Rao, et al., "A Novel, Two-Step Synthesis of 2-Methoxyestradiol" <u>Synthesis</u> , pp. 168-169 (March 1977)	
	GK	Ravindra, R., "Effect of Estradiol on the <i>in vitro</i> Assembly of Rat Brain Tubulin", <u>J. Indian Inst. Sci.</u> , Vol. 64, No. 3, pp. 27-35 (1983)	
	GL	Sakakibara et al., "Effects of Diethylstilbestrol and its Methyl Ethers on Aneuploidy Induction and Microtubule Distribution in Chinese Hamster V79 cells", <u>Mutation Research</u> , Vol. 263, pp. 269-276 (1991)	
	GM	Sato et al., "Effect of Estradiol and Ethynylestradiol on Microtubule Distribution in Chinese Hamster V79 Cells", <u>Chem. Pharm. Bull.</u> , Vol. 40, No. 1, pp. 182-184 (1992)	
B.B.	GN	Sato et al., "Disruptive Effect of Diethylstilbestrol on Microtubules", <u>Gann</u> , Vol. 75, pp. 1046-1048 (1984)	

Examiner Signature	Badio	Date Considered	3/24/03
--------------------	-------	-----------------	---------



INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 8

Complete if Known

Application Number	09/644,387
Filing Date	August 23, 2000
First Named Inventor	Greg ry Agoston, et al.
Group Art Unit	1616
Examiner Name	Badio, B.
Attorney Docket Number	05213-0541 (43170-219662)

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS

Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published

Examiner Initials	Cite No.		T ²
PB	CA	Adams, E.F. et al., "Steroidal regulation of oestradiol-17B dehydrogenase activity of the human breast cancer cell line MCF-7", <u>Journal of Endocrinology</u> , Vol. 188, pp. 149-154 (July 1988)	
	CB	Aizu-Yokota, et al., "Natural Estrogens Induce Modulation of Microtubules in Chinese Hamster V79 Cells in Culture", <u>Cancer Research</u> , Vol. 55, pp. 1863-1868 (May 1, 1995)	
	CC	Attalla, et al., "2-Methoxyestradiol Arrests Cells in Mitosis without Depolymerizing Tubulin", <u>Biochem. and Biophys. Resch. Comm.</u> , Vol. 228, pp. 467-473 (1996)	
	CD	Ayala, et al. "The Induction of Accelerated Thymic Programmed Cell Death During Polymicrobial Sepsis: Control by Corticosteroids but not Tumor Necrosis Factor", <u>Shock</u> , Vol. 3, No. 4, pp. 259-267 (April 1995) (Abstract Only)	
	CE	Banik, et al., "Orally Active Long-Acting Estrogen (3-(2-propynyloxy)-estra-1,3,5 (10) - trien - 17.beta.-ol trimethylacetate)", <u>Steroids</u> , Vol. 16, No. 3, pp.289-296 (1970) (Identifier Only)	
	CF	Bardon, et al., "Steroid Receptor-Mediated Cytotoxicity of an Antiestrogen and an Antiprogesterin in Breast Cancer Cells", <u>Cancer Researcher</u> , Vol. 47, No. 5, pp. 1441-1448 (March 1, 1987) (Abstract Only)	
	CG	Bhat, et al., "Estradiol-induced Mitotic Inhibition in the Bursa of Fabricius of Male Domestic Duckling", <u>Mikroskopie</u> , Vol. 39, pp. 113-117 (May 1982)	
	CH	Blagosklonny, et al. "Raf-1/bcl-2 Phosphorylation: A Step from Microtubule Damage to Cell Death", <u>Cancer Research</u> , Vol. 57, pp. 130-135 (January 1, 1997)	
	CI	Blickenstaff, et al., "Estrogen-Catharanthus (Vinca) Alkaloid Conjugates", <u>Cytotoxic Estrogens in Hormone Receptive Tumors</u> , Academic Press, pp. 89-105 (1980)	
	CJ	Boyé et al., "185. Deaminocolchinyll Methyl Ether: Synthesis from 2,3,4,4'-Tetramethoxybiphenyl-2-carbaldehyde. Comparison of Antitubulin Effects of Deaminocolchinyll Methyl Ether and Dehydro Analogs", <u>Helvetica Chimica Acta</u> , Vol. 72, pp. 1690-1696 (1989)	
	CK	Brodie, A.M., "Aromatase Inhibitors in the Treatment of Breast Cancer", <u>J.Steroid Biochem. Mol. Biol.</u> , Vol. 49, Nos. 4-6, pp. 281-287 (June 1994) (Abstract Only)	
	CL	Brosens, et al., "Comparative Study of the Estrogenic Effect of Ethinylestradiol and Mestranol on the Endometrium" <u>Laboratory fore Gynecological Physiopathology</u> , Vol. 14, No. 6, pp. 679-685 (December 1976)	
	CM	Castagnetta, Luigi, et al. "Simple Approach to Measure Metabolic Pathways of Steroid in Living Cells", <u>J. Chromatogr.</u> , Vol. 572, pp.25-39 (1991)	
PB	CN	Chasserot-Golaz, et al., "Biotransformation of 17.beta.-hydroxy-11.beta.-(4-dimethylaminophenyl) 17.alpha.1-propynyl-estra-4, 9-dien-3-one (RU486) in Rat Hepatoma Variants", <u>Biochem. Pharmacol.</u> , Vol. 46, No. 11, pp. 2100-2103 (1993) (Identifier Only)	

Examiner Signature	Padio	Date Considered	3/24/03
--------------------	-------	-----------------	---------



PTO/SB/08B (08-00)
Approved for use through 10/31/2002 OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO		Complete if Known			
		Application Number	09/644,387		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Filing Date	August 23, 2000		
		First Named Inventor	Gregory Agoston, et al.		
		Group Art Unit	1616		
		Examiner Name	Badio, B.		
Sheet	3	of	8	Attorney Docket Number	05213-0541 (43170-219662)

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
BB	DA	Chen, et al., "A New Synthetic Route to 2- and 4-Methoxyestradiols by Nucleophilic Substitution" <u>Steroids</u> , Vol. 47, No. 1, pp. 63-66 (January 1986)	
	DB	Chen, et al., "Synthesis of 11.beta.-(4-dimethylaminophenyl)-17.beta.-hydroxy-17.alpha.-(1-propynyl) estro-4,9-dien-3-one (RU486)", <u>Nanjing Yaoxueyuan Xuebao</u> , Vol. 17, No. 4, pp. 282-285 (1986) (Identifier Only)	
	DC	Cohen et al., "Novel Total Synthesis of (+)-Estrone 3-Methyl Ether, (+)-13B-Ethyl-3-methoxygona-1,3,5(10-triene-17-one, and (+)-Equilenin 3-Methyl Ether", <u>The Journal of Organic Chemistry</u> , Vol. 6, pp. 681-685 (March 21, 1975)	
	DD	Collins, et al., "The Structure and Function of Estrogens. XI* Synthesis of (=/-)-7(8-11 α)-abeo-Estradiol and its 9,11-Didehydro Derivative" <u>Aust. J. Chem.</u> , Vol. 45, pp. 71-97 (1992)	
	DE	Cummings, et al., "Apoptosis", <u>Am J. of Surgical Pathology</u> , Vol. 21, No. 1, pp. 88-101 (1997)	
	DF	Crum et al., "A New Class of Steroids Inhibits Angiogenesis in the Presence of Heparin or a Heparin Fragment", <u>Science</u> , Vol. 230, pp. 1375-1378 (December 20, 1985)	
	DG	Cushman, et al., "Synthesis of Analogs of 2-Methoxyestradiol with Enhanced Inhibitory Effects on Tubulin Polymerization and Cancer Cell Growth", <u>J. Med. Chem.</u> , Vol. 40, No. 15, pp. 2323-2334 (July 1997) (Abstract Only)	
	DH	Cushman, et al., "Synthesis, Antitubulin and Antimitotic Activity, and Cytotoxicity of Analogs of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite of Estradiol that Inhibits Tubulin Polymerization by Binding to the Colchicine Binding Site", <u>J. Med. Chem.</u> , Vol. 38, No. 12, pp. 2041-2049 (1995)	
	DI	D'Amato, et al., "2-Methoxyestradiol, an Endogenous Mammalian Metabolite, Inhibits Tubulin Polymerization by Interacting at the Colchicine Site", <u>Proc. Natl. Acad. Sci.</u> , Vol. 91, pp. 3964-3968 (April 1994)	
	DJ	Dvir, et al., "Thin-layer Chromatography of DANSYL-oestrogens", <u>J. Chromatog.</u> Vol. 52, pp. 505-506 (1970)	
	DK	Epe, et al., "Microtubular Proteins as Cellular Targets for Carcinogenic Estrogens and Other Carcinogens" <u>Mechanisms of Chromosome Distribution and Aneuploidy</u> , pp. 345-351 (1989)	
	DL	Evans et al., "A Convergent Total Synthesis of (+)-Colchicine and (+)-Desacetamidocolchicine", <u>J. Am. Chem. Society</u> , Vol. 103, pp. 5813-5821 (1981)	
BB	DM	Fishman, Jack, "Synthesis of 2-Methoxyestrogens", <u>J. Am. Chem. Soc.</u> , Vol. 80, pp. 1213-1216 (1958)	

Examiner Signature	<i>Badio</i>	Date Considered	3/24/03
--------------------	--------------	-----------------	---------

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.

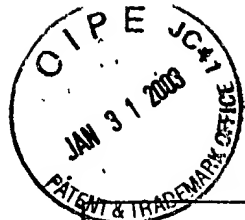


INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Compleat If Known	
		Application Number	09/644,387
		Filing Date	August 23, 2000
		First Named Inventor	Gregory Agoston, et al.
		Group Art Unit	1616
		Examiner Name	Badio, B.
Sheet 4 of 8	Attorney Docket Number	05213-0541 (43170-219662)	

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
BB	EA	Fitzgerald, "Molecular Features of Colchicine Associated with Antimitotic Activity and Inhibition of Tubulin Polymerization", <u>Biochem. Pharmacol.</u> , Vol. 25, pp. 1383-1387 (1976)	
	EB	Fotsis, et al., "The Endogenous Oestrogen Metabolite 2-Methoxyestradiol Inhibits Angiogenesis and Suppresses Tumour Growth", <u>Nature</u> , Vol. 368, pp. 237-239 (March 17, 1994)	
	EC	Getahun et al. "Synthesis of Alkoxy-Substituted Diaryl Compounds and Correlation of Ring Separation with Inhibition of Tubulin Polymerization: Differential Enhancement of Inhibitory Effects Under Suboptimal Polymerization Reaction Conditions", <u>J. Med. Chem.</u> , Vol. 35, pp. 1058-1067 (March 20, 1992)	
	ED	Gross, et al., "Inhibition of Tumor Growth, Vascularization, and Collagenolysis in the Rabbit Cornea by Medroxyprogesterone", <u>Proc. Natl. Acad. Sci. USA</u> , Vol. 78, No. 2, pp. 1176-1180 (February 1981)	
	EE	Halder, et al., "Bcl2 is the Guardian of Microtubule Integrity", <u>Cancer Research</u> , Vol. 57, pp. 229-233 (January 15, 1997)	
	EF	Hamel, et al., "Interactions of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite, with Unpolymerized Tubulin and with Tubulin Polymers", <u>Biochemistry</u> , Vol. 35, No. 4, pp.1304-1310 (1996)	
	EG	Hartley-Asp et al., "Diethylstilbestrol Induces Metaphase Arrest and Inhibits Microtubule Assembly", <u>Mutation Research</u> , Vol. 143, pp. 231-235 (1985)	
	EH	He, Hu-Ming et al., "A Versatile Synthesis of 2-Methoxyestradiol, an Endogenous Metabolite of Estradiol Which Inhibits Tubulin Polymerization by Binding to the Colchicine Binding Site" <u>Bioorg. Med. Chem. Lett.</u> , Vol. 4, No. 14, pp. 1725-1728 (1994)	
	EI	Huber, et al., "Tubulin Binding of Conformationally Restricted Bis-Aryl Compounds", <u>Bioorg. Med. Chem. Lett.</u> , Vol. 1, No. 5, pp. 243-246 (1991)	
	EJ	Josefsson, et al., "Suppression of Type II Collagen-Induced Arthritis by the Endogenous Estrogen Metabolite 2-Methoxyestradiol", <u>Arthritis & Rheumatism</u> , Vol. 40, No. 1, pp. 154-163 (January 1997)	
	EK	Kabarity, et al., "Further Investigations on the cytological effects of some contraceptives" <u>Mutation Research</u> , Vol. 135, pp. 181-188 (1984)	
	EL	Kelly, et al., "The Stimulation of Prostaglandin Production by Two Antiprogestosterone Steroids in Human Endometrial Cells" <u>J. Clin. Endocrinol Metab.</u> , Vol. 62, No. 6, pp. 1116-1123 (June 1986) (Abstract only)	
	EM	Klauber, et al., "Inhibition of Angiogenesis and Breast Cancer in Mice by the Microtubule Inhibitors 2-Methoxyestradiol and Taxol", <u>Cancer Research</u> , Vol. 57, pp. 81-86 (January 1, 1997)	
BB	EN	Le Bras, J. et al. "Activation and Regioselective Ortho-Functionalization of the A-Ring of β -Estradiol Promoted by "Cp*Ir": An Efficient Organometallic Procedure for the Synthesis of 2-Methoxyestradiol", <u>Organometallics</u> , Vol. 16, pp. 1765-1771 (1997)	

Examiner Signature	Badio	Date Considered	3/24/03
--------------------	-------	-----------------	---------

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Approved for use through 10/31/2002 OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for Form 1449/APTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	09/644,387
		Filing Date	August 23, 2000
		First Named Inventor	Gregory Agoston, et al.
		Group Art Unit	1616
		Examiner Name	Badio, B.
Sheet 5 of 8	Attorney Docket Number	05213-0541 (43170-219662)	

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	1*
BB	FA	Lilopristone/ 1-[4-(Dimethylamino)phenyl]-17-hydroxy-17-(3-hydroxy-1-propenyl) estradiol, 9-dien-3-one; ZK 98734; <u>Dictionary of Drugs</u> , (1990), <u>Dictionary of Steroids</u> , (1991), <u>Dictionary of Organic Compounds</u> (6 th Ed. 1996), <u>Dictionary of Pharmacological Agents</u> (1997) (Identifier Only)	
	FB	Lin et al., "Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: a Structure-Activity Study", <u>Molecular Pharmacology</u> , Vol. 34, No. 2, pp. 200-208 (August 1988)	
BB	FC	"Lincoln et al., "Conformation of Thiocolchicine and Two B-Ring-Modified Analogues Bound to Tubulin Studied with Optical Spectroscopy", <u>Biochemistry</u> , Vol. 30, No. 5, pp. 1179-1187 (1991)	
	FD	Lichtenauer, et al., "Zur Behandlung des Prostata-Karzinoms", <u>Deutsches Medizinisches Journal</u> , Vol. 23, pp. 148-249 (1972) <i>English translation needed</i>	
BB	FE	Lottering et al., "Effects of 17 β -Estradiol Metabolites on Cell Cycle Events in MCF-7 Cells", <u>Cancer Research</u> , Vol. 52, pp. 5926-5932 (November 1, 1992)	
	FF	Lottering, et al., "17 β -Estradiol Metabolites Affect Some Regulators of the MCF-7 Cell Cycle", <u>Cancer Letters</u> , Vol. 110, pp. 181-186 (1996)	
	FG	Meikrantz, et al., "Apoptosis and the Cell Cycle", <u>J. of Cellular Biochem.</u> Vol. 58, pp. 160-174 (1995)	
	FH	Miller, et al., "Synthesis and Structure-Activity Profiles of A-Homoestrans, the Estratropenes", <u>J. Med. Chem.</u> , Vol. 40, pp. 3836-3841 (1997)	
	FI	Miller, Thomas Allen "Tubulin as a Therapeutic Target", <u>DAI-B</u> , Vol. 59, No. 7, p. 3454 (January 1999) (Abstract Only)	
BB	FJ	Morgan, et al., "Calcium and Oestrogen Interactions upon the Rat Thymic Lymphocyte Plasma Membrane", <u>Biochemical and Biophysical Research Communications</u> , Vol. 72, No. 2, pp. 663-672 (September 20, 1976)	
	FK	Morgan, et al., CA 85:172052, 1976 <i>copy not provided</i>	
BB	FL	Mukhopadhyay, et al. "Induction of Apoptosis in Human Lung Cancer Cells after Wild-Type p53 Activation by Methoxyestradiol", <u>Oncogene</u> , Vol. 14, pp. 379-384 (1997)	
	FM	Mukundan et al., "Liver Regeneration in Oral Contraceptive Treated Female Rats - Effects of Moderate Malnutrition", <u>Hormone and Metabolic Research</u> , Vol. 16, pp. 641-645 (December 1984)	
	FN	Nakamura et al., "Studies on the Total Synthesis of <i>dl</i> -Colchicine. I. Synthesis of 3-Hydroxy-9, 10, 11-trimethoxy-1,2,3,4,6,7-hexahydro-5H-dibenzo[a,c] cycloheptatrien-5-one", <u>Chem. Pharm. Bull.</u> , Vol. 10, pp. 281-290 (1962)	
BB	FO	Nakagawa-Yagi, et al., "The Endogenous Estrogen Metabolite 2-Methoxyestradiol Induces Apoptotic Neuronal Cell Death <i>In Vitro</i> ", <u>Life Sciences</u> , Vol. 58, No. 17, pp. 1461-1467 (1996)	

Examiner Signature	Badio	Date Considered	3/24/03
--------------------	-------	-----------------	---------

*Unique citation designation number. *Applicant is to place a check mark here if English language translation is attached.



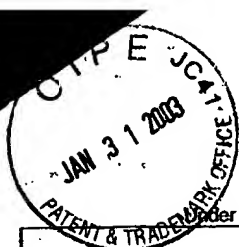
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO			Complete if Known		
			Applicati n Number	09/644,387	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Filing Date	August 23, 2000	
			First Named Inventor	Gregory Agoston, et al.	
			Group Art Unit	1616	
			Examiner Name	Badio, B.	
			Attorney Docket Number	05213-0541 (43170-219662)	
Sheet	7	of	8		

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published		T ²
BB	HA ✓	Sawada et al., "Colchicine-Like Effect of Diethylstilbestrol (DES) on Mammalian Cells in Vitro", <u>Mutation Research</u> , Vol. 57, pp. 175-182 (1978)		
	HB ✓	Seegers, J. C. et al., "The Cytotoxic Effects of Estradiol-17β, Catecholestradiols and Methoxyestradiols on Dividing MCF-7 and HeLa Cells", <u>J. Steroid Biochem</u> , Vol. 32, No. 6, pp. 797-809 (1989)		
	HC ✓	Sharp et al., "Diethylstilboestrol: the Binding and Effects of Diethylstilboestrol upon the Polymerisation and Depolymerisation of Purified Microtubule Protein <i>in vitro</i> ", <u>Carcinogenes</u> , Vol. 6, No. 6, pp. 865-871 (1985)		
	HD ✓	Spicer et al., "Catecholestrogens Inhibit Proliferation and DNA Synthesis of Porcine Granulosa Cells in Vitro: Comparison with Estradiol, 5α-dihydrotestosterone, Gonadotropins and Catecholamines", <u>Molecular and Cellular Endocrinology</u> , Vol. 64, pp. 119-126 (1989)		
	HE ✓	Sternlicht et al., "Colchicine Inhibition of Microtubule Assembly via Copolymer Formation", <u>The Journal of Biological Chemistry</u> , Vol. 254, No. 20, pp. 10540-10550 (1979)		
	HF ✓	Sun et al., "Antitumor Agents. 139. Synthesis and Biological Evaluation of Thiocolchicine Analogs 5, 6-Dihydro-6(S)-(acyloxy)- and 5,6-Dihydro-6(S)-[(acyloxy)methyl]-1,2,3-trimethoxy-9-(methylthio)-8H-cyclohepta[a]naphthalene-8-ones as Novel Cytotoxic and Antimitotic Agents.", <u>J. Med. Chem.</u> , Vol. 36, pp. 544-551 (1993)		
	HG ✓	Sunagawa et al., "Synthesis of Colchicine; Synthesis of <i>dl</i> -Demethoxydeoxy-hexahydrocolchicine", <u>Chem. Pharm. Bull.</u> , Vol. 9, pp. 81-83 (1961)		
	HH ✓	Teranishi, Masonori, et al., "Methylation of Catechol Estrogen with Diazomethane", <u>Chem. Pharm. Bull.</u> , Vol. 31, No.9, pp. 3309-3314 (1983)		
	HI ✓	Tishler, et al., "Microtubule-Active Drugs Taxol, Vinblastine, and Nocodazole Increase the Levels of Transcriptionally Active p53", <u>Cancer Research</u> , Vol. 55, pp. 6021-6025 (December 15, 1995)		
	HJ ✓	Tsutsui et al., "Comparison of Human Versus Syrian Hamster Cells in Culture for Induction of Mitotic Inhibition, Binucleation and Multinucleation, Following Treatment with Four Aneuploidogens", <u>Toxic in Vitro</u> , Vol. 4, No. 1, pp. 75-84 (1990)		
	HK ✓	Utne, T., et al. "The Synthesis of 2-and 4-Fluoroestadiol", <u>Journal of Organic Chemistry</u> , Vol. 33, No. 6, pp. 2469-2473 (June 1968)		
	HL ✓	Van Geerestein, et al. "Structure of 11.beta.-(4-(dimethylamino)phenyl)-17.beta.-hydroxy-17.alpha.-(2-propenyl)estra-4, 9-dien-3-one, <u>Acta Crystall Ogr., Sect. C: Cryst. Struct. Commun.</u> , Vol. C43, No. 2, pp.319-322 (1987) (Identifier Only)		
BB	HM ✓	Van Tamelen et al., "The Synthesis of Colchicine", <u>Tetrahedron</u> , Vol. 14, p. 8-34 (1961)		

Examiner Signature	<i>Badio</i>	Date Considered	2/24/03
--------------------	--------------	-----------------	---------

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.



Substitute for Form 1449/APTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	09/644,387
		Filing Date	August 23, 2000
		First Named Inventor	Gregory Agoston, et al.
		Group Art Unit	1616
		Examiner Name	Badio, B.
		Attorney Docket Number	05213-0541 (43170-219662)
Sheet 8	of 8		

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T*
BB	IA	Wang, Zhiqiang, et al., "An Optimized Synthesis of 2-Methoxyestradiol, a Naturally Occurring Human Metabolite with Anticancer Activity" <u>Synth. Commun.</u> Vol. 28, No. 23, pp. 4431-4437 (1998)	
	IB	Wheeler, W. J. et al., "Mitotic Inhibition and Aneuploidy Induction by Naturally Occurring and Synthetic Estrogens in Chinese Hamster Cells in Vitro", <u>Mutation Research</u> , Vol. 171, pp. 31-41 (1986)	
	IC	Wheeler, W. J. et al., "Mitotic Inhibition and Chromosome Displacement Induced by Estradiol in Chinese Hamsters Cells", <u>Cell Motility and the Cytoskeleton</u> , Vol. 7, No. 3, pp. 235-247 (1987)	
	ID	Yue, et al., "2-Methoxyestradiol, an Endogenous Estrogen Metabolite, Induces Apoptosis in Endothelial Cells and Inhibits Angiogenesis: Possible Role for Stress-Activated Protein Kinase Signaling Pathway and Fas Expression", <u>Molecular Pharm.</u> Vol. 51, pp. 951-962 (1997)	
	IE	Guangrong, et al., "Effect of Components of Crown Ether Copper(I)Iodide Mixed Catalyst on Nucleophilic Substitution of Bromoestrogen" <u>Chemical Abstracts</u> , Vol. 111, No. 21, Abstract No. 195225, page 818, Column 1, (November 20, 1989)	
	IF	<u>The Merck Index</u> , 11 th Edition, paragraphs 583-584, pp. 88 (1989)	
	IG	Ochs, et al., "Effect of Tumor Promoting Contraceptive Steroids on Growth and Drug Metabolizing Enzymes in Rat Liver", <u>Cancer Res.</u> , Vol. 46, No. 3, pp. 1224-1232 (1986) (Abstract)	
BB	IH	Mayol, et al., "Ethinylestradiol- Induced Cell Proliferation in Rat Liver Involvement of Specific Populations of Hepatocytes", <u>Carcinogenesis</u> , Vol. 12, No. 12, pp. 2381-2388 (1992) (Abstract)	

Examiner Signature	Badio	Date Considered	3/24/03
--------------------	-------	-----------------	---------